

Application No. PCT/CA2004/001794  
Amendment dated

## **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions and listings of claims in the application:

### **Listing of Claims:**

1. (original) A modified virus ablated of its natural receptors interactions with an unmodified or non-naturally occurring cell, said modified virus comprising a non-native polypeptide, said modified virus having an altered tropism conferred by said non-native peptide, and replicating only in cells that can interact with said non-native peptide, said virus being incapable of infecting a cell through a CAR-dependent entry pathway.
2. (original) The modified virus of claim 1, which is derived from a virus selected from the group consisting of adenovirus, retrovirus, lentivirus, adeno-associated virus, Reoviridae, Picornaviridae, Parvoviridae, Papovaviridae and Caliciviridae.
3. (currently amended) The modified virus of claim 1 ~~or 2~~, which is derived from human adenovirus.
4. (currently amended) The modified virus of ~~any one of claims 1 to 3~~, which is derived from human adenovirus serotype 2 or 5.
5. (currently amended) The modified virus of ~~any one of claims 1 to 4~~, wherein said non-native polypeptide replaces, is incorporated into, or forms a fusion protein with, a viral protein component of the wild type virus.
6. (original) The modified virus of claim 5, wherein said viral protein component is an adenoviral fiber protein.

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7. (original) The modified virus of claim 6, wherein said non-native polypeptide is incorporated into an adenoviral fiber protein such that the wild-type fiber knob or cell binding domain thereof is removed.

8. (currently amended) The modified virus of ~~any one of claims 1 to 7~~, wherein said non-native polypeptide is or comprises a combinatorial protein or an affibody.

9. (currently amended) The modified virus of ~~any one of claims 1 to 8~~, wherein said non-native polypeptide comprises one or more sequence from a bacterial receptor ligand.

10. (currently amended) The modified virus of ~~any one of claims 1 to 8~~, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:1.

11. (currently amended) The modified virus of ~~any one of claims 1 to 8~~, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:2.

12. (currently amended) The modified virus of ~~any one of claims 1 to 11~~, wherein said non-native polypeptide binds a non-naturally occurring production cell or permissive cell.

13. (currently amended) The modified virus of ~~any one of claims 1 to 12~~, further comprising a retargeting adapter comprising: i) a binding moiety for binding the non-native polypeptide and ii) a further binding moiety of a receptor for retargeting said virus on cells expressing said receptor.

14. (original) The modified virus of claim 13, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:1 and said binding moiety for binding the non-native polypeptide comprises at least one repeat of SEQ ID NO:2.

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15. (original) The modified virus of claim 13, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:2 and said binding moiety for binding the non-native polypeptide comprises at least one repeat of SEQ ID NO:1.

16. (currently amended) The modified virus of ~~any one of claims 13 to 16~~, wherein said adapter binds to the non-native polypeptide through non-covalent physical forces selected from the group consisting of van der Waals forces, electrostatic forces, stacking interactions, hydrogen bonding and steric fit.

17. (currently amended) The modified virus of ~~any one of claims 1 to 12~~, wherein said non-native polypeptide comprises a cleavage site positioned in a location that enables a further binding moiety of a receptor to be added on the modified virus for retargeting said virus on cells expressing said receptor.

18. (original) The modified virus of claim 17, wherein the binding moiety is capable of binding to a cell specific ligand.

19. (currently amended) The modified virus of ~~any one of claims 1 to 18~~, which further comprises a site for insertion of one or more desired therapeutic genes or nucleic acid molecules.

20. (currently amended) A cell containing a modified virus as defined in ~~any one of claims 1 to 19~~.

21. (currently amended) A permissive cell for a modified virus as defined in ~~any one of claims 1 to 19~~, which is capable of being cultured to propagate said modified virus.

22. (currently amended) A non-naturally occurring permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide as defined in ~~any one of claims 1 to 19~~.

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23. (original) A non-naturally occurring permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide as defined in claim 10, wherein said surface receptor comprises at least one copy of the amino acid sequence as set forth in SEQ ID NO:2.

24. (original) A non-naturally occurring permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide as defined in claim 11, wherein said surface receptor comprises at least one copy of the amino acid sequence as set forth in SEQ ID NO:1.

25. (currently amended) A method for producing a modified virus as defined in ~~any one of claims 1 to 19~~ in cell culture, comprising the steps of: i) genetically modifying a virus to produce a modified virus ablated of its natural receptors interactions with an unmodified or non-naturally occurring cell, said modified virus comprising a non-native polypeptide, said modified virus having an altered tropism conferred by said non-native peptide, and replicating only in cells that can interact with said non-native peptide; ii) infecting permissive cells with said modified virus; and iii) culturing said cells to produce the virus.

26. (original) The method of claim 25, further comprising a step of iv) harvesting the modified virus produced.

27. (original) The method of claim 26, further comprising a step of v) purifying the modified virus produced.

~~28.(cancelled) The modified virus of any one of claims 1 to 19 for use in therapy.~~

~~29.(cancelled) Use of the modified virus of any one of claims 1 to 19 in the preparation of a medicament for the treatment of tumor cells or proliferating cells.~~

31-28. (currently amended) A pharmaceutical composition comprising a modified virus as defined in ~~any one of claims 1 to 19~~ and a pharmaceutically acceptable carrier or excipient.

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~~31-29.~~ (currently amended) A reagent kit comprising: i) a modified virus as defined in any one of claims 1-19 and ii) a permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide, said cell being capable of being infected by said modified virus.~~as defined in any one of claims 20 to 24.~~

~~32-29.~~ (currently amended) A medicament or a precursor thereof comprising a virus as defined in ~~any one of claims 1 to 19.~~